

General

Guideline Title

Brachytherapy for patients with prostate cancer: American Society of Clinical Oncology/Cancer Care Ontario joint guideline update.

Bibliographic Source(s)

Chin J, Rumble RB, Kollmeier M, Heath E, Efsthathiou J, Dorff T, Berman B, Feifer A, Jacques A, Loblaw DA. Brachytherapy for patients with prostate cancer: American Society of Clinical Oncology/Cancer Care Ontario joint guideline update. *J Clin Oncol*. 2017 May 20;35(15):1737-43. [22 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Rodrigues G, Yao X, Loblaw A, Brundage M, Chin J, Genitourinary Cancer Disease Site Group. Low-dose rate brachytherapy for patients with low- or intermediate-risk prostate cancer. Toronto (ON): Cancer Care Ontario (CCO); 2012 Oct 31. 55 p. (Evidence-based series; no. 3-10). [165 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Guideline Questions

1. In patients with newly diagnosed prostate cancer, what is the efficacy of brachytherapy alone for clinical outcomes compared with external beam radiation therapy (EBRT) alone or radical prostatectomy (RP) alone?
2. In patients with newly diagnosed prostate cancer, what is the efficacy of brachytherapy combined with EBRT for clinical outcomes compared with brachytherapy alone, EBRT alone, or RP alone?
3. Among the isotopes used for low-dose rate (LDR) brachytherapy (e.g., iodine-125 [^{125}I], palladium-103 [^{103}Pd], and cesium-131 [^{131}Cs]), which isotope maximizes clinical outcomes when used in patients with newly diagnosed prostate cancer?

Updated Recommendations

- For patients with low-risk prostate cancer who require or choose active treatment, LDR alone, EBRT alone, or RP should be offered to eligible patients.
- For patients with intermediate-risk prostate cancer choosing EBRT with or without androgen-deprivation therapy (ADT), brachytherapy boost (LDR or high-dose rate [HDR]) should be offered to eligible patients. For low-intermediate risk prostate cancer (Gleason 7,

prostate-specific antigen, 10 ng/mL or Gleason 6, prostate-specific antigen, 10 to 20 ng/mL) LDR brachytherapy alone may be offered as monotherapy. For patients with high-risk prostate cancer receiving EBRT and ADT, brachytherapy boost (LDR or HDR) should be offered to eligible patients.

- ^{125}I and ^{103}Pd are each reasonable isotope options for patients receiving LDR brachytherapy; no recommendation can be made for or against using ^{131}Cs or HDR monotherapy.
- Patients should be encouraged to participate in clinical trials to test novel or targeted approaches to this disease.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Prostate cancer

Guideline Category

Treatment

Clinical Specialty

Nuclear Medicine

Oncology

Radiation Oncology

Surgery

Urology

Intended Users

Physicians

Guideline Objective(s)

- To provide oncologists, other health care practitioners, patients, and caregivers with recommendations regarding the use of brachytherapy for patients with prostate cancer that includes the most recent evidence
- To consider new evidence on the use of brachytherapy and determine if the original recommendations of the Cancer Care Ontario (CCO) guideline remain valid or if updates are warranted

Target Population

Patients with newly diagnosed prostate cancer who require or choose active treatment and are not considering, or are not suitable for, active surveillance

Interventions and Practices Considered

1. Low-dose rate brachytherapy alone
2. External beam radiation therapy (EBRT) alone
3. Radical prostatectomy (RP) alone
4. EBRT (with or without androgen-deprivation therapy) combined with brachytherapy boost (LDR or high-dose rate [HDR])
5. Iodine-125 (^{125}I) and palladium-103 (^{103}Pd) isotope options
6. Participation in clinical trials

Note: Cesium-131 (^{131}Cs) and HDR monotherapy were considered, but no recommendation can be made.

Major Outcomes Considered

- Biochemical disease-free survival
- Biochemical failure
- Clinical failure
- Overall survival
- Progression-free survival
- Metastasis-free survival
- Prostate cancer-specific mortality
- Toxicity (genitourinary, gastrointestinal)
- Quality of life

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Guideline Update Process

The American Society of Clinical Oncology (ASCO) uses a "signals" approach to facilitate guideline updating. This approach is intended to identify new, potentially practice-changing data—signals—that might translate into revised practice recommendations. The approach relies on routine literature searching and the expertise of ASCO guideline panel members to identify signals. The Methodology Supplement (see the "Availability of Companion Documents" field) provides additional information about the signals approach.

For this update, the signal was the presentation of a randomized controlled trial (RCT) comparing dose-escalated (DE)-external beam radiation therapy (EBRT) with low-dose rate (LDR) brachytherapy boost (LDR-B) that could potentially expand the patient population to whom the original recommendations would apply. The full Update Committee was then convened to review the evidence.

Evidence was also collected through a systematic review of the medical literature. Publications were included if they were phase III randomized clinical trials of brachytherapy compared with either external beam radiation therapy (EBRT) or radical prostatectomy (RP) in men with prostate cancer. These publications were identified by rerunning the original strategy in MEDLINE, EMBASE, and the Cochrane database of systematic reviews, for the period from the original search in 2011 through to the end of August 2015. A final search for important papers was made in December 2016.

Further details on the search strategy and results are provided in Data Supplements 2 and 3 (see the "Availability of Companion Documents" field).

Number of Source Documents

Of the 32 publications identified, six publications (addressing five randomized controlled trials [RCTs]) met the eligibility criteria and form the

evidence base for this update.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Guide for Rating of Potential for Bias

Rating of Potential for Bias	Definitions for Rating Potential for Risk of Bias in Randomized Controlled Trials
Low risk	No major features in the study that risk biased results, and none of the limitations are thought to decrease the validity of the conclusions. The study avoids problems such as failure to apply true randomization, selection of a population unrepresentative of the target patients, high dropout rates, and no intention-to-treat analysis; and key study features are described clearly (including the population, setting, interventions, comparison groups, measurement of outcomes, and reasons for dropouts).
Intermediate	The study is susceptible to some bias, but flaws are not sufficient to invalidate the results. Enough of the items introduce some uncertainty about the validity of the conclusions. The study does not meet all the criteria required for a rating of good quality, but no flaw is likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.
High risk	There are significant flaws that imply biases of various types that may invalidate the results. Several of the items introduce serious uncertainty about the validity of the conclusions. The study has serious errors in design, analysis, or reporting; large amounts of missing information; or discrepancies in reporting.

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Extraction

Literature search results were reviewed and deemed appropriate for full text review by one American Society of Clinical Oncology (ASCO) staff reviewer in consultation with the Panel Co-Chairs. Data were extracted by one staff reviewer and subsequently checked for accuracy through an audit of the data by another ASCO staff member. Disagreements were resolved through discussion and consultation with the Co-Chairs if necessary. Evidence tables are provided in the Data Supplement (see the "Availability of Companion Documents" field).

Study Quality Assessment

Study quality was formally assessed for the studies identified. Design aspects related to the individual study quality were assessed by one reviewer and included factors such as blinding, allocation concealment, placebo control, intention to treat, funding sources, etc. The risk of bias is assessed as "low," "intermediate," or "high" for most of the identified evidence.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Update Panel Composition

The American Society of Clinical Oncology (ASCO) Clinical Practice Guidelines Committee (CPGC) and Cancer Care Ontario (CCO) Program in Evidence-based Care (PEBC) convened an Update Panel with multidisciplinary representation in radiation oncology, medical oncology, urology, patient/advocacy representation, and guideline implementation. The Update Panel was led by two Co-Chairs (one from each organization) who had primary responsibility for the development and timely completion of the guideline. For this guideline product, the Co-Chairs selected additional members to assist in the development and review of the guideline drafts.

Guideline Development Process

The Update Panel held teleconferences on several occasions and corresponded frequently through e-mail; progress on guideline development was driven primarily by the Co-Chairs along with ASCO staff. The purpose of the meetings was for members to contribute content, provide critical review, interpret evidence, and finalize the guideline recommendations based upon the consideration of the evidence. All members of the Update Panel participated in the preparation of the draft guideline document.

Development of Recommendations

The guideline recommendations were crafted, in part, using the GuideLines Into DEcision Support (GLIDES) methodology and accompanying BRIDGE-Wiz software.TM This method helps Guideline Expert Panels systematically develop clear, translatable, and implementable recommendations using natural language, based on the evidence and assessment of its quality to increase usability for end users. The process incorporates distilling the actions involved, identifying who will carry them out, to whom, under what circumstances, and clarifying if and how end users can carry out the actions consistently. This process helps the Expert Panel focus the discussion, avoid using unnecessary and/or ambiguous language, and clearly state its intentions.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Cost Considerations

The American Society of Clinical Oncology (ASCO) recognizes that there is often a wide array of choices for treating many cancer types, with often a wide disparity in cost to patients and payers (despite much difference in effectiveness or toxicity). One study reported that of the radiation modalities used in the treatment of prostate cancer, from the Medicare payer perspective, low-dose rate (LDR) brachytherapy is the cheapest (compared with stereotactic ablative body radiotherapy [SABR], external beam radiation therapy [EBRT], or protons). Another study showed that in the Canadian health care context, SABR had the higher quality-adjusted life-years and was more cost effective compared with LDR (and both were better than EBRT). Further work is needed to articulate cost, cost-effectiveness, and cost-utility differences between the various prostate cancer treatment approaches.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

All members of the Update Panel participated in the preparation of the draft guideline document, which was then disseminated for external review and submitted to the *Journal of Clinical Oncology* (JCO) for peer review and consideration for publication. All American Society of Clinical Oncology (ASCO) guidelines are reviewed and approved by the ASCO Clinical Practice Guideline Committee prior to publication. This joint guideline update was also reviewed and approved by Cancer Care Ontario's (CCO's) Report Approval Panel (RAP).

The ASCO Clinical Practice Guideline Committee approved this update on November 21, 2016. The CCO RAP approved the update on December 1, 2016.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The updated recommendations are supported by randomized controlled trials (RCTs).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Appropriate use of all management options (radical prostatectomy [RP], external beam radiation therapy [EBRT], and brachytherapy alone or in combination) for treatment of prostate cancer
- Provision of optimum treatment strategies to reduce the burden of disease in this patient population

Potential Harms

Genitourinary (GU) and gastrointestinal (GI) toxicities were reported in the five randomized controlled trials reviewed for this update. See Table 2 (Adverse Effects) and the discussion of early and late GU and GI toxicities in the original guideline document.

Contraindications

Contraindications

Patients ineligible for brachytherapy may include: moderate to severe baseline urinary symptoms, large prostate volume, medically unfit, prior transurethral resection of the prostate, and contraindications to radiation treatment.

Qualifying Statements

Qualifying Statements

Guideline Disclaimers

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- This is the most recent information as of the publication date. For the most recent information, and to submit new evidence, please visit

www.asco.org/Brachytherapy-guideline and the ASCO Guidelines Wiki (www.asco.org/guidelineswiki).

- Care has been taken in the preparation of the information contained herein. Nevertheless, any person seeking to consult the report or apply its recommendations is expected to use independent medical judgment in the context of individual clinical circumstances or to seek out the supervision of a qualified clinician. Cancer Care Ontario (CCO) makes no representations or guarantees of any kind whatsoever regarding the report content or its use or application and disclaims any responsibility for its use or application in any way.
- Refer to the "Limitations of the Research" section of the original guideline document for additional qualifying information.

See the original guideline document for qualifying statements related to each recommendation.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Patient Resources

Quick Reference Guides/Physician Guides

Slide Presentation

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Chin J, Rumble RB, Kollmeier M, Heath E, Efsthathiou J, Dorff T, Berman B, Feifer A, Jacques A, Loblaw DA. Brachytherapy for patients with prostate cancer: American Society of Clinical Oncology/Cancer Care Ontario joint guideline update. *J Clin Oncol*. 2017 May 20;35(15):1737-43. [22 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2017 May 20

Guideline Developer(s)

American Society of Clinical Oncology - Medical Specialty Society

Cancer Care Ontario - State/Local Government Agency [Non-U.S.]

Guideline Developer Comment

The Program in Evidence-based Care (PEBC) is a Province of Ontario initiative sponsored by Cancer Care Ontario (CCO) and the Ontario Ministry of Health and Long-Term Care.

Source(s) of Funding

American Society of Clinical Oncology (ASCO)

The Program in Evidence-based Care (PEBC) is a provincial initiative of Cancer Care Ontario (CCO) supported by the Ontario Ministry of Health and Long-Term Care. All work produced by the PEBC is editorially independent from the Ontario Ministry of Health and Long-Term Care.

Guideline Committee

Brachytherapy for Patients With Prostate Cancer Joint Guideline Update Panel

Composition of Group That Authored the Guideline

Update Panel Members: Joseph Chin, MD (*Co-chair*, CCO), London Health Sciences Centre, London, Ontario, Canada; D. Andrew Loblaw, MD (*Co-chair*, ASCO), Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada; Marisa Kollmeier, MD (ASCO) Memorial Sloan-Kettering Cancer Center, New York, NY; Elizabeth Heath, MD (ASCO); Karmanos Cancer Institute, Detroit, MI; Jason Efstathiou, MD, DPhil (ASCO) Massachusetts General Hospital, Boston, MA; Tanya Dorff, MD (ASCO), USC Norris Cancer Center, Los Angeles, CA; Andrew Feifer, MD (CCO), Trillium Health Partners' Fidani Cancer Centre, University Health Network, Toronto, Ontario, Canada; Barry Berman, MD, PGIN (ASCO), Broward Health, Fort Lauderdale, FL; Arthur Jacques[†], patient representative Toronto, Ontario, Canada

Abbreviations: ASCO, American Society of Clinical Oncology; CCO, Cancer Care Ontario; PGIN, Practice Guideline Implementation Network.

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Financial Disclosures/Conflicts of Interest

Guideline and Conflicts of Interest

The Update Panel was assembled in accordance with American Society of Clinical Oncology's (ASCO's) Conflict of Interest Management Procedures for Clinical Practice Guidelines "Procedures," summarized at <http://www.asco.org/rwc> (). Members of the Panel completed ASCO's disclosure form, which requires disclosure of financial and other interests that are relevant to the subject matter of the guideline, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria; consulting or

advisory role; speaker's bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Procedures, the majority of the members of the Panel did not disclose any such relationships.

Authors' Disclosures of Potential Conflicts of Interest

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Patents, Royalties, Other Intellectual Property: Prostate immobilization device (GU-Lok)

Travel, Accommodations, Expenses: Janssen Oncology, Amgen, Astellas Pharma

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Rodrigues G, Yao X, Loblaw A, Brundage M, Chin J, Genitourinary Cancer Disease Site Group. Low-dose rate brachytherapy for patients with low- or intermediate-risk prostate cancer. Toronto (ON): Cancer Care Ontario (CCO); 2012 Oct 31. 55 p. (Evidence-based series; no. 3-10). [165 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available in from the [Journal of Clinical Oncology Web site](#) .

Availability of Companion Documents

The following are available:

- Brachytherapy for patients with prostate cancer: American Society of Clinical Oncology/Cancer Care Ontario joint guideline update. Methodology supplement. Alexandria (VA): American Society of Clinical Oncology; 2017. 18 p. Available from the [Journal of Clinical Oncology Web site](#) .
- Brachytherapy for patients with prostate cancer: American Society of Clinical Oncology/Cancer Care Ontario joint guideline update. Data supplements. Alexandria (VA): American Society of Clinical Oncology; 2017. 9 p. Available from the [Journal of Clinical Oncology Web site](#) .
- Brachytherapy for patients with prostate cancer: American Society of Clinical Oncology/Cancer Care Ontario joint guideline update. Slide set. Alexandria (VA): American Society of Clinical Oncology; 2017. 14 p. Available in [PDF](#) and [PowerPoint](#) formats from the American Society of Clinical Oncology (ASCO) Web site.
- Brachytherapy for patients with prostate cancer: American Society of Clinical Oncology/Cancer Care Ontario joint guideline update. Summary of recommendations. Alexandria (VA): American Society of Clinical Oncology; 2017. 2 p. Available from the [ASCO Web site](#) .
- Chin J, Rumble RB, Loblaw DA. Brachytherapy for patients with prostate cancer: American Society of Clinical Oncology/Cancer Care Ontario joint guideline update summary. J Oncol Pract. 2017 Jun;13(6):392-4. Available to subscribers from the [Journal of Oncology Practice Web site](#) .

Patient Resources

The following is available:

- Prostate cancer. 2017. Available from the [Cancer.Net Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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